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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,205	01/04/2001	Xiangzhong Yang	UCON-150	4832

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EXAMINER
AFREMOVA, VERA

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/02/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/755,205	Yang et al
Examiner	**Art Unit**
Vera Afremova	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 25, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4 and 9-35* is/are pending in the application.

4a) Of the above, claim(s) *10-35* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4 and 9* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4,5*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-4, 9-27 as amended and new claims 28-35 are pending.

Claims 5-8 were canceled by applicants in the Paper No. 9 filed 3/25/2002.

Election/Restriction

Applicants' election with traverse of Group I (claims 1-4) in Paper No. 8 filed 3/20/2002 is acknowledged.

The traversal is on the ground(s) that some groups are classified in the same class and subclass and, thus, should be examined together. Applicants argued that the "elected" subject matter (claims 1-4) would necessarily involve an overlapping search of the subject matter of the presently amended claim 9. This argument is found persuasive and claims 1-4 and 9 will be examined together. Applicants further argue that "non-elected" subject matter of the claims 10-18 and of the claims 19-26 would necessarily involve an overlapping search of the subject matter as presently amended , and, thus, the claims 10-18 and 19-26 should be examined together. Applicants appear to admit that the methods of claims 1-4 and 9 and the methods of claims 10-18 and 19-26 are of a different scope. Further, it is noted that the references which would be applied to the subject matter of claims 1-4 and 9 would not necessarily anticipate or render obvious the subject matter of claims 10-18 and 19-26, for example, they encompass nuclear transfer (see claim 11) and production of cloned embryos and animals (claims 12-18 and 20-26). The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having

materially different issues also exists. Clearly different searches and issues are involved with each group.

Newly submitted claims 28-35 are directed to an invention that is independent or distinct from the elected invention because they are directed to a particular apparatus or device which allows for rapid vitrification and to method of using this device. This device is not particularly adapted to the elected method and it is classified in class 435, subclass 283.1, for example. Accordingly, claims 10-35 are withdrawn from consideration as being directed to non-elected invention, there being no allowable generic or linking claim. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-4 and 9 are under examination in the instant office action.

Claim Rejections - 35 USC § 112

Claims 1-4 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered indefinite by the phrases "sufficient to protect against ice formation to the glass transition temperature". These phrase are confusing and the meaning is not particularly clear. For example: it is unclear what is protected. Is solution protected?

Claim 1 is indefinite because it is not particularly clear whether microdroplets of vitrification solution contain biological material or the "vitrification solution-rinsed biological material" is separated from vitrification solution during formation of droplets.

Claims 1 and 9 are indefinite because the difference between "solid surface with heat conductivity" and "solid cryogenic surface" with "thermal conductivity" which are characterized by about the same values is unclear in the method for vitrification or cryopreservation of biological material. Further, it is also uncertain what substitute "improvement" in the method of claim 9 over the method of claim 1, for example. Does the method of claim 9 avoid the use of "cryoprotective equilibration solution"?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,780,295 [IDS-4-2] taken with Steponkus et al. [IDS-4-6], Martino et al. [IDS-5-11], Yang et al. [IDS-5-21] and Papis et al. [IDS-5-22].

Claims are directed to a method for vitrification and cryopreservation of biological material wherein the method comprises step of suspending the biological material in an equilibration solution containing cryoprotectant, step of rinsing the equilibrated biological material in a vitrification solution with cryoprotectant, step of dropping the vitrification solution-rinsed biological material in a form of droplets onto solid surface which has thermal conductivity

and which has temperature of about - 150°C to about - 180°C and step of removing the frozen microdroplets. The microdroplets have size of about 10 μL and less. The equilibration solution contains less cryoprotectant than the vitrification solution. The conductivity of the solid surface has a particular value. Some claims are further drawn to the use of biological material such as cells, oocytes or embryos.

US 5,780,295 [IDS-4-2] teaches a method for vitrification and cryopreservation of biological material wherein the method comprises step of suspending and rinsing the biological material in solutions containing cryoprotectants, step of dropping the solutions with the biological material in a form of microdroplets onto a solid cryogenic surface which is cooled to about - 160°C and step of removing the frozen microdroplets (col. 4, lines 17-24). The cited patent teaches the use of a cryogenic surface which has high thermal conductivity as metal and which allows to achieve high cooling rate and to avoid thermal shock of biological material (col. 7, lines 7-12). The cited patent teaches the use of microdroplets which have size of about 25 μL to about 250 μL and it teaches that the smaller size is preferential in order to achieve maximum cooling rate and short drying time (col.6, lines 32-37). The patent discloses the use of various solutions with cryoprotectant at various concentration (col. 8). The cited patent teaches the use of various biological materials including cells, sperm and isles (col. 4, lines 55-60) but it is lacking the disclosure related to oocytes and embryos.

However, the references by Steponkus et al. [IDS-4-6] (see description under fig. 1) and Martino et al. [IDS-5-11] (see abstract and page 1061, col. 1, last paragraph) disclose methods

for vitrification and cryopreservation of embryos and oocytes wherein the method comprises two step pretreatment of biological materials with equilibration and vitrification solutions containing different concentrations of cryoprotectants and step of dropping the treated biological material in a form of microdroplets onto solid copper surface for rapid cooling and freezing and step of removing the frozen microdroplets. Steponkus et al teach the use of microdroplets having size of about 20 μL an the use of copper cryogenic surface cooled by liquid propane. Martino et al teach the use of microdroplets having size of less that 1 μL and the use of copper cryogenic surface which is immediately plunged into liquid nitrogen after formation of microdroplets.

The other cited references by Yang et al. [IDS-5-21] and Papis et al. [IDS-5-22] are relied upon for the disclosure of methods for vitrification and cryopreservation of biological material including mammalian oocytes and zygotes by ultra-rapid cooling intended to avoid chilling injury of the biological material wherein the methods encompasses the use of both equilibration and vitrification solutions and the use of microdroplets having various sizes depending on type of biological material such as about 10 μL for bovine zygotes and about 6 μL for bovine oocytes (see abstracts).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute oocytes or embryos of the secondary references [Steponkus et al., Martino et al.,,Yang et al.,Papis et al.] for a generic biological material in the method for vitrification and cryopreservation of US '295 which encompass the ultra-rapid cooling on a solid cryogenic surface with a reasonable expectation of success in vitrification and

cryopreservation of oocytes and/or embryos because it is known to freeze oocytes and embryos on solid copper grids designed for ultra-rapid cooling [Steponkus et al., Martino et al.] which allows to avoid chilling injury and obtained satisfactory results for future oocyte fertilization and embryo development as taught by the secondary references [Steponkus et al., Martino et al., Yang et al., Papis et al.]. One of skill in the art would have been motivated to decrease sizes of microdroplets because the prior art teaches that the smaller size is preferential in order to achieve maximum cooling rate and short drying time [US'295] and the use of microdroplets of sizes such as about 10 μL and less have been demonstrated in the prior art [Martino et al., Yang et al., Papis et al.]. Although the cited references are silent with regard to a particular value of the thermal conductivity of solid surfaces used in the method for cryopreservation, the materials which are used are metals and they are characterized by high thermal conductive properties sufficient to achieve rapid cooling and to avoid chilling injury of biological materials as taught by the references. The particular heat conductivity which is claimed is the same as that of a metal (specification page 7, line 7). Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

Art Unit 1651

June 20, 2002.

PRIMARY EXAMINER